10/828,278

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S76	282	514/255.06	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/12 10:34
S77	68	S76 AND (AMILORIDE OR (SODIUM ADJ CHANNEL) OR PYRAZINOYLGUANIDINE)	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	ON	2006/12/12 10:37
S78	1	("6858614").PN.	USPAT	OR	OFF	2006/12/12 10:35
S79	1	("6858615").PN.	USPAT	OR	OFF	2006/12/12 10:36
S80	1	("6903105").PN.	USPAT	OR	OFF	2006/12/12 10:36
S81	1	("7064129").PN.	USPAT	OR	OFF	2006/12/12 10:37
S82	1	("7030117").PN.	USPAT	OR	OFF	2006/12/12 10:37
S83	1	("6995160").PN.	USPAT	OR	OFF	2006/12/12 10:37
S84	1	("7026325").PN.	USPAT	OR	OFF	2006/12/12 10:37

RELATED PATENTS

10/828,278

STN SEARCH TRANSCRIPT

```
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 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  AUG 09  INSPEC enhanced with 1898-1968 archive
 NEWS  4  AUG 28  ADISCTI Reloaded and Enhanced
 NEWS  5  AUG 30  CA(SM)/CAplus(SM) Austrian patent law changes
 NEWS  6  SEP 11  CA/CAplus enhanced with more pre-1907 records
 NEWS  7  SEP 21  CA/CAplus fields enhanced with simultaneous left and right
                  truncation
 NEWS  8  SEP 25  CA(SM)/CAplus(SM) display of CA Lexicon enhanced
 NEWS  9  SEP 25  CAS REGISTRY(SM) no longer includes Concord 3D coordinates
 NEWS 10  SEP 25  CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
 NEWS 11  SEP 28  CEABA-VTB classification code fields reloaded with new
                  classification scheme
 NEWS 12  OCT 19  LOGOFF HOLD duration extended to 120 minutes
 NEWS 13  OCT 19  E-mail format enhanced
 NEWS 14  OCT 23  Option to turn off MARPAT highlighting enhancements available
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                  multiple databases
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 NEWS 17  OCT 30  CHEMLIST enhanced with new search and display field
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 NEWS 19  NOV 10  CA/CAplus F-Term thesaurus enhanced
 NEWS 20  NOV 10  STN Express with Discover! free maintenance release Version
                  8.01c now available
 NEWS 21  NOV 13  CA/CAplus pre-1967 chemical substance index entries enhanced
                  with preparation role
 NEWS 22  NOV 20  CAS Registry Number crossover limit increased to 300,000 in
                  additional databases
 NEWS 23  NOV 20  CA/CAplus to MARPAT accession number crossover limit increased
                  to 50,000
 NEWS 24  NOV 20  CA/CAplus patent kind codes will be updated
 NEWS 25  DEC 01  CAS REGISTRY updated with new ambiguity codes
 NEWS 26  DEC 11  CAS REGISTRY chemical nomenclature enhanced

 NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

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FILE 'HOME' ENTERED AT 10:58:59 ON 12 DEC 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
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Choice (Y/n):
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
index.  Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of
commands which can be used in this file.

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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STRUCTURE FILE UPDATES:   11 DEC 2006  HIGHEST RN 915185-72-7
DICTIONARY FILE UPDATES:  11 DEC 2006  HIGHEST RN 915185-72-7

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Uploading C:\Program Files\Stnexp\Queries\SODIUM CHANNEL PYRAZINE DIV METHODS.str
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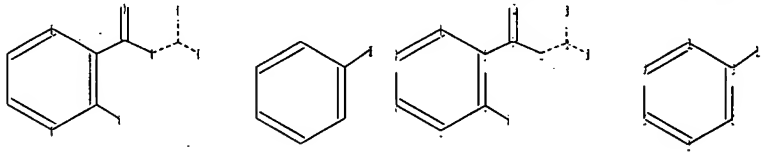

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7  9  10  11  12  13  14  21
ring nodes :
1  2  3  4  5  6  15  16  17  18  19  20
chain bonds :
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5-9 6-7 9-10 9-11 11-12 12-13 12-14 19-21
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
6-7 9-10 9-11 11-12 12-13 12-14 19-21
exact bonds :
5-9
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
isolated ring systems :
containing 1 : 15 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
 20:Atom 21:CLASS

L1 STRUCTURE UPLOADED

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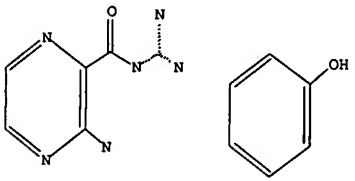
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SEARCH INITIATED 11:00:59 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 55 TO ITERATE

100.0% PROCESSED 55 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH **COMPLETE**
PROJECTED ITERATIONS: 656 TO 1544
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 11:01:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1179 TO ITERATE

100.0% PROCESSED 1179 ITERATIONS 26 ANSWERS
SEARCH TIME: 00.00.01

L3 26 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 167.38 167.59

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FILE LAST UPDATED: 11 Dec 2006 (20061211/ED)

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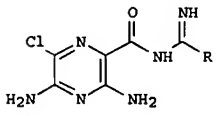
=> s l3
L4 9 L3

=> d 1-9 ibib abs hitstr

L4 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:593381 CAPLUS
DOCUMENT NUMBER: 145:211000
TITLE: Design, Synthesis, and Structure-Activity Relationships of Novel 2-Substituted Pyrazinoylguanidine Epithelial Sodium Channel Blockers: Drugs for Cystic Fibrosis and Chronic Bronchitis
AUTHOR(S): Hirsh, Andrew J.; Molino, Bruce F.; Zhang, Jianzhong; Astakhova, Nadezhda; Geiss, William B.; Sargent, Bruce J.; Swenson, Brian D.; Usyatinsky, Alexander; Wyle, Michael J.; Boucher, Richard C.; Smith, Rick T.; Zamurs, Andra; Johnson, M. Ross
CORPORATE SOURCE: Parion Sciences Inc., Durham, NC, 27713, USA
SOURCE: Journal of Medicinal Chemistry (2006), 49(14), 4098-4115
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



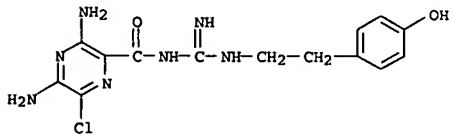
I

AB Amiloride, the prototypical epithelial sodium channel (ENaC) blocker, has been administered with limited success as aerosol therapy for improving pulmonary function in patients with the genetic disorder cystic fibrosis. This study was conducted to synthesize and identify more potent, less reversible ENaC blockers, targeted for aerosol therapy and possessing minimal systemic renal activity. A series of novel 2-substituted acylguanidine analogs of amiloride were synthesized and evaluated for potency and reversibility on bronchial ENaC. All compds. tested were more potent and less reversible at blocking sodium-dependent short-circuit current than amiloride. Compds. I [R = NH(CH2)4C6H4O(CH2)2OH-4, NH(CH2)4C6H4O(CH2)3OH-4, NH(CH2)4C6H4OCH2CH(OH)CH2OH-4 (both R and S isomers)] showed the greatest potency on ENaC with IC50 values below 10 nM. A regioselective difference in potency was found, whereas no stereospecific difference in potency on ENaC was displayed. Lead compound I [R = NH(CH2)4C6H4OCH2CH(OH)CH2OH-4 (racemic)] was 102-fold more potent and 5-fold less reversible than amiloride and displayed the lowest IC50 value ever reported for an ENaC blocker.

IT 905292-80-0
RL: PAC (Pharmacological activity); BIOL (Biological study)
(design, synthesis, and structure-activity relationships of 2-substituted pyrazinoylguanidine epithelial sodium channel blockers as potential drugs for cystic fibrosis and chronic bronchitis)

RN 905292-80-0 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[2-(4-hydroxyphenyl)ethyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

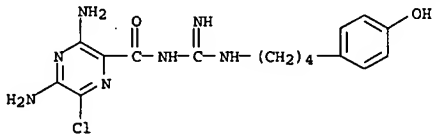


● HCl

IT 583825-15-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis, and structure-activity relationships of 2-substituted pyrazinoylguanidine epithelial sodium channel blockers as potential drugs for cystic fibrosis and chronic bronchitis)

RN 583825-15-4 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

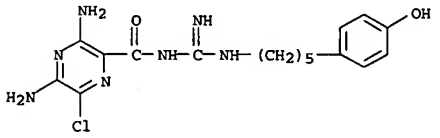


● HCl

IT 583825-17-6P 583825-19-8P 583825-33-6P
905292-81-1P 905292-83-3P 905292-84-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis, and structure-activity relationships of 2-substituted pyrazinoylguanidine epithelial sodium channel blockers as potential drugs for cystic fibrosis and chronic bronchitis)

RN 583825-17-6 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[5-(4-hydroxyphenyl)pentyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 583825-19-8 CAPLUS

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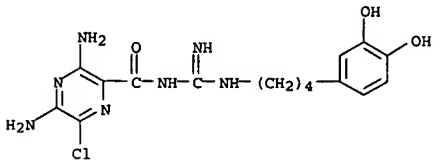
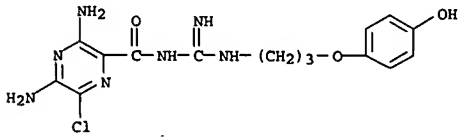


● HCl

RN 583825-33-6 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4-

hydroxyphenoxy)propyl]amino]iminomethyl]-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

RN 905292-81-1 CAPLUS
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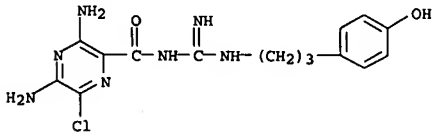

● HCl

RN 905292-83-3 CAPLUS
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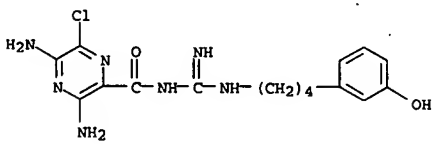
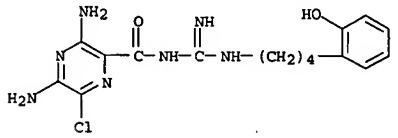


● HCl

RN 905292-84-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2-hydroxyphenyl)butyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:325702 CAPLUS
DOCUMENT NUMBER: 142:367646
TITLE: Methods using sodium channel blockers for reducing risk of infection from pathogens
INVENTOR(S): Johnson, Michael R.; Hopkins, Samuel E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 52 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Ref. APPN

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005080093	A1	20050414	US 2004-920484	20040818
AU 2004287352	A1	20050519	AU 2004-287352	20040819
CA 2534069	AA	20050519	CA 2004-2534069	20040819
WO 2005044180	A2	20050519	WO 2004-US26778	20040819
WO 2005044180	A3	20051006		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1656022	A2	20060517	EP 2004-816810	20040819
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.:
US 2003-496482P P 20030820
US 2004-920484 A 20040818
WO 2004-US26778 W 20040819

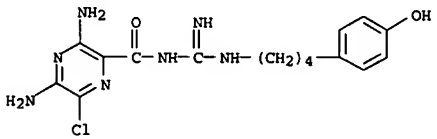
OTHER SOURCE(S): MARPAT 142:367646

AB Prophylactic treatment methods are provided for protection of individuals and/or populations against infection from airborne pathogens. In particular, prophylactic treatment methods are provided comprising administering a sodium channel blocker or pharmaceutically acceptable salt thereof to one or more members of a population at risk of exposure to or already exposed to one or more airborne pathogens, either from natural sources or from intentional release of pathogens into the environment.

IT 583825-14-3 583825-15-4 583825-16-5

583825-18-7 583825-23-4 583825-25-6
849588-70-1 849588-71-2 849588-72-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sodium channel blockers for reducing risk of infection from pathogens)

RN 583825-14-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 583825-15-4 CAPLUS
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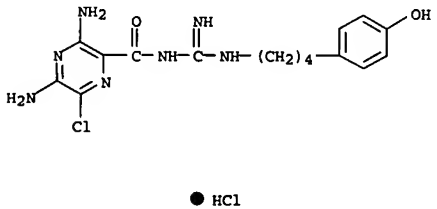
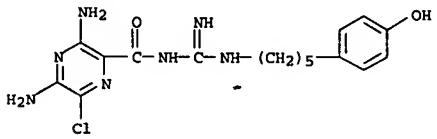


● HCl

RN 583825-16-5 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[5-(4-hydroxyphenyl)pentyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 583825-18-7 CAPLUS
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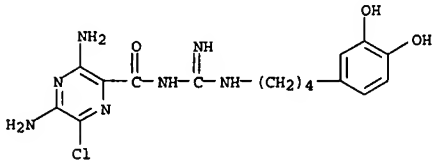

RN 583825-23-4 CAPLUS
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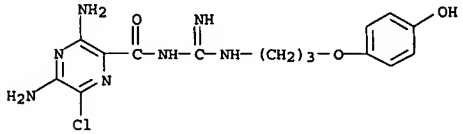

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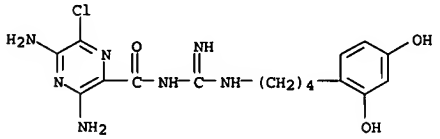

RN 849588-70-1 CAPLUS
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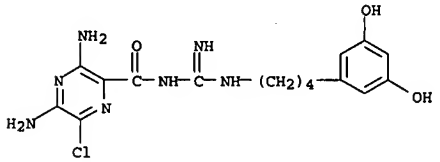
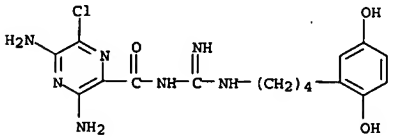
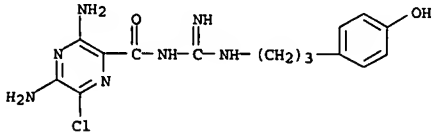


RN 849588-71-2 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(2,5-dihydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 849588-72-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4-hydroxyphenyl)propyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:678615 CAPLUS
DOCUMENT NUMBER: 139:191482
TITLE: Sodium channel blockers
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

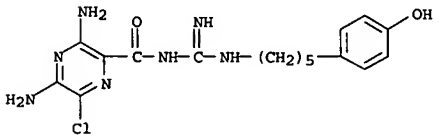
APPLICANT

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070184	A2	20030828	WO 2003-US4823	20030219
WO 2003070184	A3	20040617		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003195160	A1	20031016	US 2002-76551	20020219
US 6858614	B2	20050222		
CA 2476837	AA	20030828	CA 2003-2476837	20030219
AU 2003215286	A1	20030909	AU 2003-215286	20030219
EP 1485359	A2	20041215	EP 2003-711105	20030219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005526726	T2	20050908	JP 2003-569144	20030219
US 2004198744	A1	20041007	US 2004-828278	20040421
US 2004198745	A1	20041007	US 2004-828329	20040421
US 2004198746	A1	20041007	US 2004-828353	20040421
US 2004198747	A1	20041007	US 2004-828354	20040421
US 2004204424	A1	20041014	US 2004-828235	20040421
PRIORITY APPLN. INFO.:			US 2002-76551	A 20020219
			WO 2003-US4823	W 20030219

OTHER SOURCE(S): MARPAT 139:191482

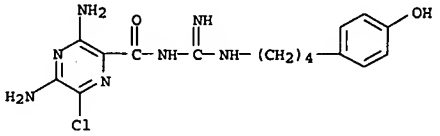
AB The present invention relates to sodium channel blockers (Markush structures are included). The present invention also includes a variety of methods of treatment using these novel sodium channel blockers.

IT 583825-17-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(sodium channel blockers for therapy of pulmonary and other diseases)
RN 583825-17-6 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[5-(4-hydroxyphenyl)pentyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

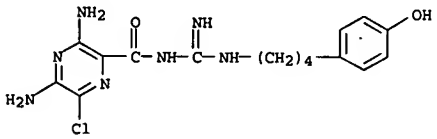


● HCl

IT 583825-14-3P 583825-15-4P 583825-16-5P
583825-18-7P 583825-19-8P 583825-23-4P
583825-24-5P 583825-25-6P 583825-26-7P
583825-33-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sodium channel blockers for therapy of pulmonary and other diseases)
RN 583825-14-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



RN 583825-15-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 583825-16-5 CAPLUS
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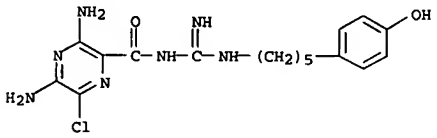
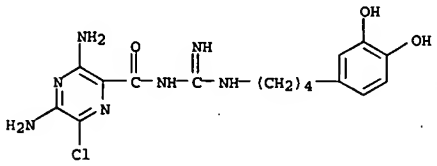


RN 583825-18-7 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(3,4-dihydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



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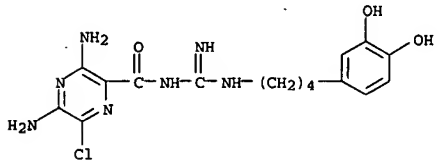

● HCl

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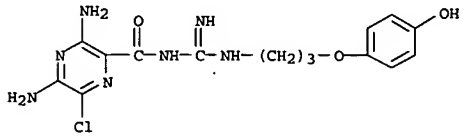
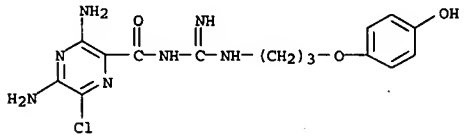


RN 583825-24-5 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[3-(4-hydroxyphenoxy)propyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

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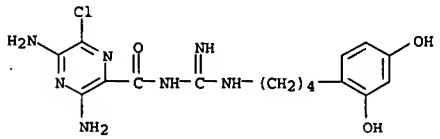

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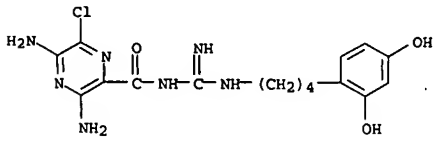

● HCl

RN 583825-33-6 CAPLUS
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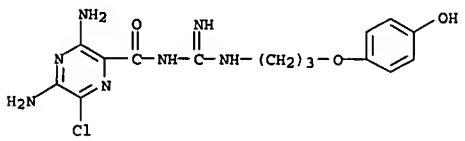

● HBr

L4 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:678613 CAPLUS
DOCUMENT NUMBER: 139:214488
TITLE: Preparation of diaminopyrazines as sodium channel blockers for promoting the hydration of mucosal surfaces
INVENTOR(S): Johnson, Michael R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

RELATED APP'N.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070182	A2	20030828	WO 2003-US4817	20030219
WO 2003070182	A3	20031224		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003199456	A1	20031023	US 2002-76571	20020219
US 6858615	B2	20050222		
CA 2476430	AA	20030828	CA 2003-2476430	20030219
AU 2003211135	A1	20030909	AU 2003-211135	20030219
EP 1485360	A2	20041215	EP 2003-742810	20030219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005530692	T2	20051013	JP 2003-569142	20030219
US 2004198748	A1	20041007	US 2004-828466	20040421
US 2004198749	A1	20041007	US 2004-828479	20040421
US 2004204425	A1	20041014	US 2004-828352	20040421
US 2004229884	A1	20041118	US 2004-828171	20040421
US 2006142306	A1	20060629	US 2005-532110	20050421
PRIORITY APPLN. INFO.:			US 2002-76571	A 20020219
			WO 2003-US4817	W 20030219

OTHER SOURCE(S): MARPAT 139:214488
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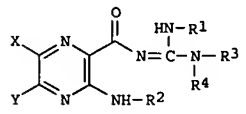

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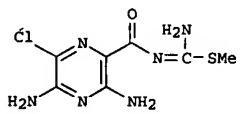
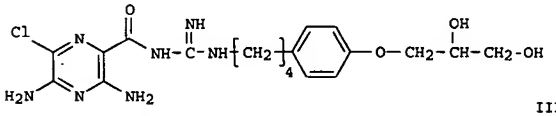


II



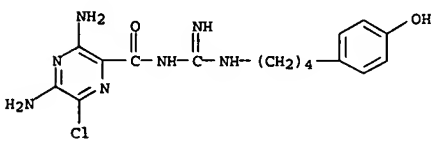
III

AB Title compds. I [X = H, halo, CF3, etc.; Y = H, OH, SH, etc.; R1 = H, alkyl; R2 = R7, (CH2)mOR8, (CH2)mNR7R10, etc.; R3, R4 = H, alkyl, hydroxyalkyl, etc. with provisos; R7 = H, alkyl; R8 = H, alkyl, glucuronide, etc.; R10 = H, SO2CH3, CO2R7, etc.; m = 1-7] and their pharmaceutically acceptable salts were prepared For example, condensation of thiourea II hydroiodide and 4-[(2,3-dihydroxypropyloxy)phenyl]butylamine, e.g., prepared from 4-(4-hydroxyphenyl)butylamine in 4-steps, afforded diaminopyrazine III hydrochloride in 53% yield. In canine bronchial epithelia sodium channel blocking activity assays, 12-examples of compds. I exhibited fold-enhancement values relative to amiloride ranging from 11.2-124, e.g., the fold-enhancement value of diaminopyrazine III hydrochloride was 124. Compds. I are claimed useful as antiasthmatics, laxatives, antihypertensives, etc.

IT 583825-15-4P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of diaminopyrazines as sodium channel blockers for promoting the hydration of mucosal surfaces)

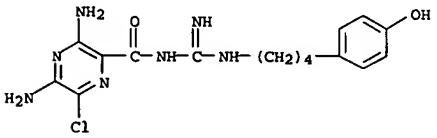
RN 583825-15-4 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]-, monohydrochloride (9CI) (CA

INDEX NAME)

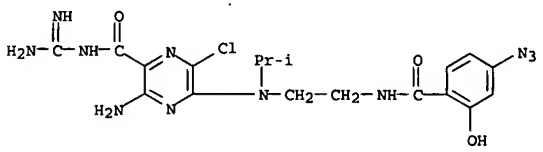


● HCl

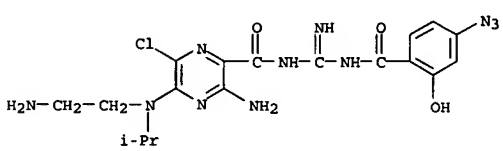
IT 583825-14-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of diaminopyrazines as sodium channel blockers for promoting the hydration of mucosal surfaces)
RN 583825-14-3 CAPLUS
CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[4-(4-hydroxyphenyl)butyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:605669 CAPLUS
DOCUMENT NUMBER: 117:205669
TITLE: Novel amiloride analog allosterically modulates the α2-adrenergic receptor but does not inhibit sodium/hydrogen ion exchange
AUTHOR(S): Wilson, Amy L.; Womble, Scott N.; Prakash, Chandra; Cragoe, E. J., Jr.; Blair, Ian A.; Limbird, Lee E.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37332-6600, USA
SOURCE: Molecular Pharmacology (1992), 42(2), 175-9
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two novel amiloride analogs have been synthesized during the course of efforts to develop a photoaffinity label for the amiloride allosteric domain on α2-adrenergic receptors. One of these, 5-[N-2'-aminoethyl-N'-isopropyl]amiloride-N-[4"-azidosalicylamide] (A-EIA-AS), markedly accelerates the rate of dissociation of [3H]yohimbine from affinity-purified α2-adrenergic receptors, an assay for allosteric modulation of receptor-adrenergic ligand interactions. In contrast, this agent does not appreciably inhibit Na+/H+ exchange, measured as 5-(N-ethyl-N-isopropyl)amiloride (EIA)-inhibitable 22Na+ uptake into cultured renal epithelial cells. A second analog, 5-[N'-2'-(4"-azidosalicylamidino)ethyl-N'-isopropyl]amiloride (ASA-EIA), does not foster an accelerated rate of dissociation of [3H]yohimbine binding from the α2 receptor but does block the ability of A-EIA-AS to do so, suggesting that ASA-EIA and A-EIA-AS interact at a common binding site. Interestingly, the ability of EIA to accelerate [3H]yohimbine dissociation is not blocked by ASA-EIA, a finding that may indicate that EIA and A-EIA-AS allosterically modulate α2 receptor-ligand interactions via distinct or nonoverlapping binding sites.
IT 144176-47-6 144176-48-7
RL: BIOL (Biological study)
(adrenergic receptor modulation by, hydrogen ion-sodium exchange in relation to)
RN 144176-47-6 CAPLUS
CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[[2-[(4-azido-2-hydroxybenzoyl)amino]ethyl](1-methylethyl)amino]-6-chloro- (9CI) (CA INDEX NAME)



RN 144176-48-7 CAPLUS
CN Pyrazinecarboxamide, 3-amino-5-[(2-aminoethyl)(1-methylethyl)amino]-N-[[(4-azido-2-hydroxybenzoyl)amino]iminomethyl]-6-chloro- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:441425 CAPLUS
DOCUMENT NUMBER: 115:41425
TITLE: Reversal of intrinsic multidrug resistance in Chinese hamster ovary cells by amiloride analogs
AUTHOR(S): Epand, R. F.; Epand, R. M.; Gupta, R. S.; Cragoe, E. J., Jr.
CORPORATE SOURCE: Health Sci. Cent., McMaster Univ., Hamilton, ON, L8N 3Z5, Can.
SOURCE: British Journal of Cancer (1991), 63(2), 247-51
CODEN: BJCAAI; ISSN: 0007-0920
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of amiloride analogs can sensitize wild type Chinese hamster ovary (CHO) cells to the cytotoxic action of vinblastine, daunomycin, puromycin or colchicine. Some of these analogs also have weak sensitizing effects on the multidrug resistant CHO cell line, CHRC5. The unusual feature of most of the active amiloride analogs is that they are more potent in reversing the intrinsic multidrug resistance (MDR) phenotype of CHO cells than their acquired MDR characteristic. Human HeLa cells that do not exhibit intrinsic MDR are not affected by these agents. Several of the amiloride analogs have a greater effect in increasing adriamycin uptake in wild type CHO cells than they do with CHRC5 cells. The differential

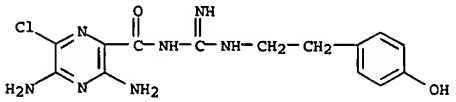
THIS IS THE CLOSEST ART. IT IS PROVIDED OUT OF OA'S OF 10/828,208 THOUGH.

effect of amiloride analogs on intrinsic vs. acquired MDR characteristics of Chinese hamster cells suggests some differences in the underlying resistance mechanisms.

IT 134788-24-2
RL: BIOL (Biological study)
(multiple resistance to neoplasm inhibitors inhibition by)

RN 134788-24-2 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[2-(4-hydroxyphenyl)ethyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:402710 CAPLUS

DOCUMENT NUMBER: 113:2710

TITLE: Photoactivatable probe for the sodium/hydrogen ion exchanger cross-links a 66-kDa renal brush border membrane protein

AUTHOR(S): Ross, Willie; Bertrand, William; Morrison, Aubrey

CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA

SOURCE: Journal of Biological Chemistry (1990), 265(10), 5341-4
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

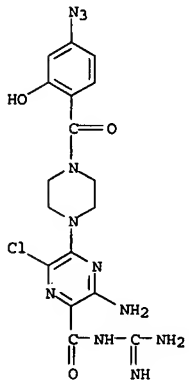
LANGUAGE: English

AB Earlier studies on LLC-PK1 cells have demonstrated 2 pharmacol. distinct Na+/H+ exchangers in renal epithelia. In addition, the cDNA clone for the human Na+/H+ antiporter which is growth factor activatable has been isolated and expressed (Sardet, C., et al., 1989). Here the synthesis of an amiloride analog that can be photoactivated and labeled with 125I is reported. This analog covalently crosslinks a 66-kDa protein of bovine renal brush border membranes. A rabbit polyclonal antibody that was directed against a 20-amino acid peptide of the cytoplasmic domain of its human Na+/H+ antiporter also gives a pos. Western against 66-kDa protein of bovine brush border membranes. Thus, the photoactive probe may be helpful in the isolation and purification of the brush border Na+/H+ exchanger.

IT 127628-92-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and radioiodonation of)

RN 127628-92-6 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-(4-azido-2-hydroxybenzoyl)-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)

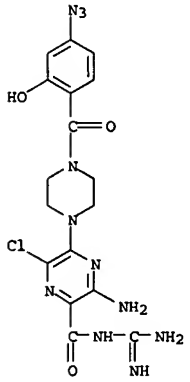


IT 127513-40-0P
RL: PREP (Preparation)
(preparation of, as photoactivable probe for sodium-hydroxy ion exchanger)

RN 127513-40-0 CAPLUS

CN Pyrazinecarboxamide, 3-amino-N-(aminoiminomethyl)-5-[4-[4-azido-2-hydroxy-3(or 5)-(iodo-125I)benzoyl]-1-piperazinyl]-6-chloro- (9CI) (CA INDEX NAME)

PAGE 1-A



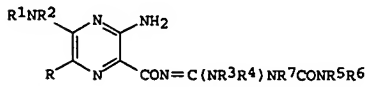
PAGE 2-A

D1—^{125}I

L4 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1978:509585 CAPLUS
DOCUMENT NUMBER: 89:109585
TITLE: Pyrazinecarboxamides
INVENTOR(S): Cragoe, Edward J., Jr.; Woltersdorf, Otto W., Jr.; Habecker, Charles N.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 15 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4085211	A	19780418	US 1976-722442	19760913
DK 7605314	A	19770616	DK 1976-5314	19761125
SE 7613289	A	19770616	SE 1976-13289	19761126
SE 431452	B	19840206		
SE 431452	C	19840517		
NL 7613276	A	19770617	NL 1976-13276	19761129
AU 7620181	A1	19780608	AU 1976-20181	19761202
AU 511429	B2	19800821		
ES 454160	A1	19780301	ES 1976-454160	19761210
FR 2335226	A1	19770715	FR 1976-37459	19761213
FR 2335226	B1	19790309		
GB 1527297	A	19781004	GB 1976-51940	19761213
HU 175504	P	19800828	HU 1976-ME2034	19761213
CH 630369	A	19820615	CH 1976-15660	19761213
BE 849379	A1	19770614	BE 1976-173235	19761214
ZA 7607431	A	19780726	ZA 1976-7431	19761214
JP 52106877	A2	19770907	JP 1976-149889	19761215
JP 62038350	B4	19870817		
ES 465742	A1	19781001	ES 1978-465742	19780103
PRIORITY APPLN. INFO.:			US 1975-640803	A2 19751215

OTHER SOURCE(S): MARPAT 89:109585
GI



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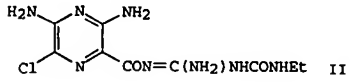
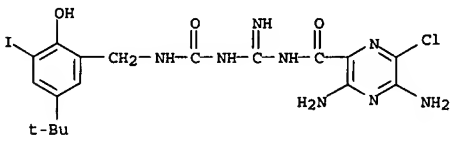


II

AB A series of title amides I (R = halo; R1 = H, alkyl, cycloalkyl, alkenyl; R2 = H, alkyl; NR1R2 = pyrrolidino, piperidino; R3 = H, alkyl, cycloalkyl; R4 = H, alkyl, cycloalkyl; R5 = H, alkyl, cycloalkyl, Ph, substituted phenyl; R6 = H, alkyl, cycloalkyl; NR5R6 = morpholino, piperazino; R7 = H, alkyl; R3R7 = CH2CH2, substituted ethylene) were prepared and are useful as diuretics (no data). Thus, the addition reaction of N-amidino-3,5-diamino-6-chloro-2-pyrazinecarboxamide with EtNCO gave II.

IT 64077-96-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 64077-96-9 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[[[[5-(1,1-dimethylethyl)-2-hydroxy-3-iodophenyl]methyl]amino]carbonyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1977:517906 CAPLUS
DOCUMENT NUMBER: 87:117906
TITLE: Pyrazinecarboxamides
INVENTOR(S): Cragoe, Edward Jethro, Jr.; Woltersdorf, Otto William, Jr.; Habecker, Charles Newcomer
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Ger. Offen., 71 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2656374	A1	19770616	DE 1976-2656374	19761213
DE 2656374	C2	19890810		
DK 7605314	A	19770616	DK 1976-5314	19761125
SE 7613289	A	19770616	SE 1976-13289	19761126
SE 431452	B	19840206		
SE 431452	C	19840517		
NL 7613276	A	19770617	NL 1976-13276	19761129
AU 7620181	A1	19780608	AU 1976-20181	19761202
AU 511429	B2	19800821		
ES 454160	A1	19780301	ES 1976-454160	19761210
FR 2335226	A1	19770715	FR 1976-37459	19761213
FR 2335226	B1	19790309		
GB 1527297	A	19781004	GB 1976-51940	19761213
HU 175504	P	19800828	HU 1976-ME2034	19761213
CH 630369	A	19820615	CH 1976-15660	19761213
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ZA 7607431	A	19780726	ZA 1976-7431	19761214
JP 52106877	A2	19770907	JP 1976-149889	19761215
JP 62038350	B4	19870817		
ES 465742	A1	19781001	ES 1978-465742	19780103
PRIORITY APPLN. INFO.:			US 1975-640803	A 19751215

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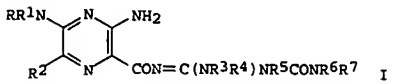

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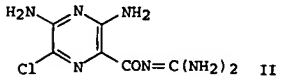


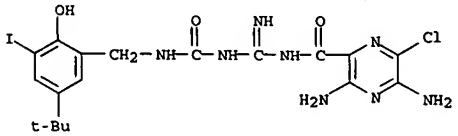
II

AB Diuretic (no data) pyrazinecarboxamides I (R, R1, R3, R4, R5, R7 = H, alkyl; R2 = halo; R6 = H, alkyl, aryl) (>60 compds.) were prepared Thus II was treated with PrNCO to give I (R, R1, R3, R4, R5, R7 = H, R2 = Cl, R6 = Pr).

IT 64077-96-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 64077-96-9 CAPLUS

CN Pyrazinecarboxamide, 3,5-diamino-6-chloro-N-[[[[[[5-(1,1-dimethylethyl)-2-hydroxy-3-iodophenyl]methyl]amino]carbonyl]amino]iminomethyl]- (9CI) (CA INDEX NAME)



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LOGOFF? (Y)/N/HOLD: